

K1532

I

II

III

IV

V

VI

VII

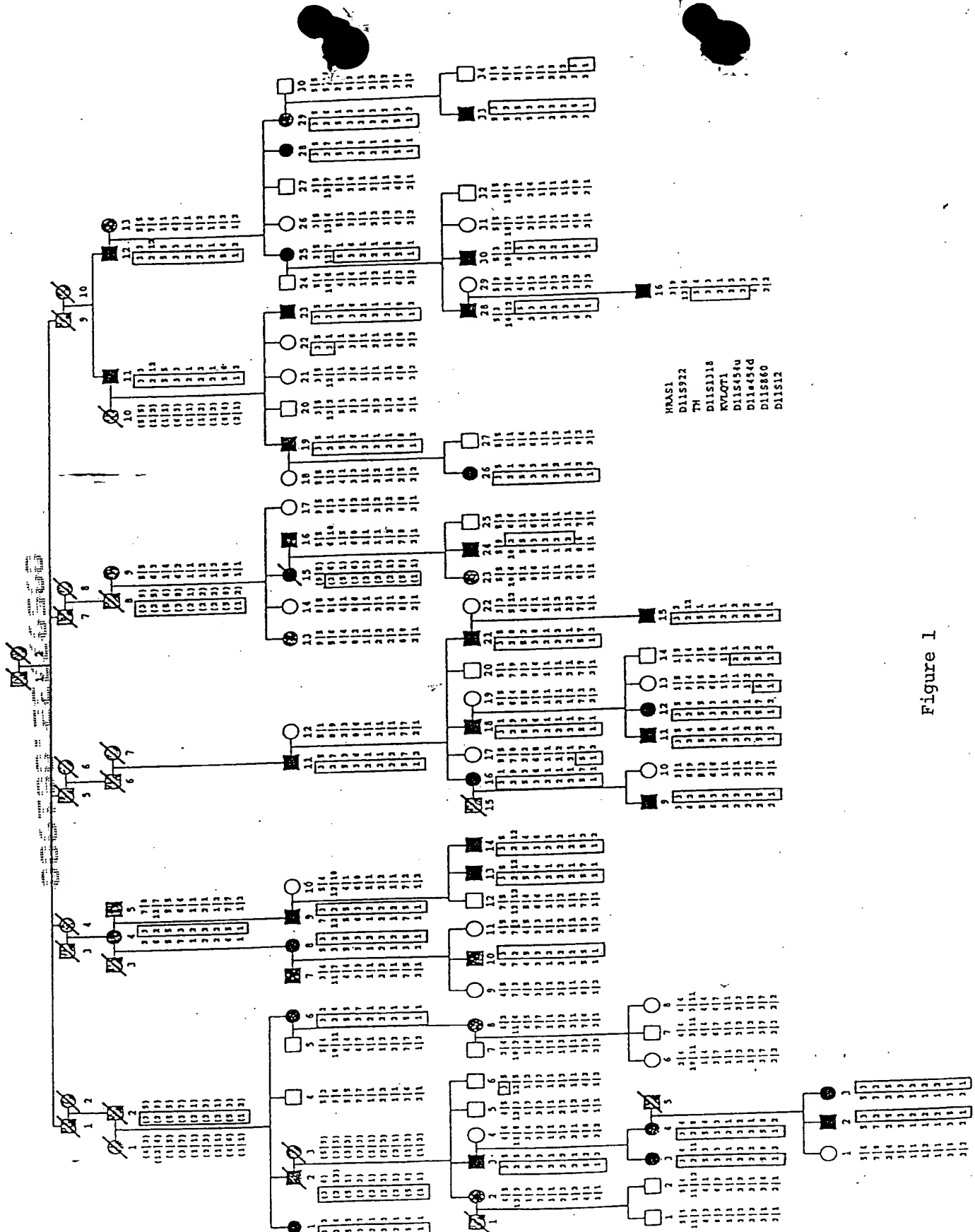


Figure 1

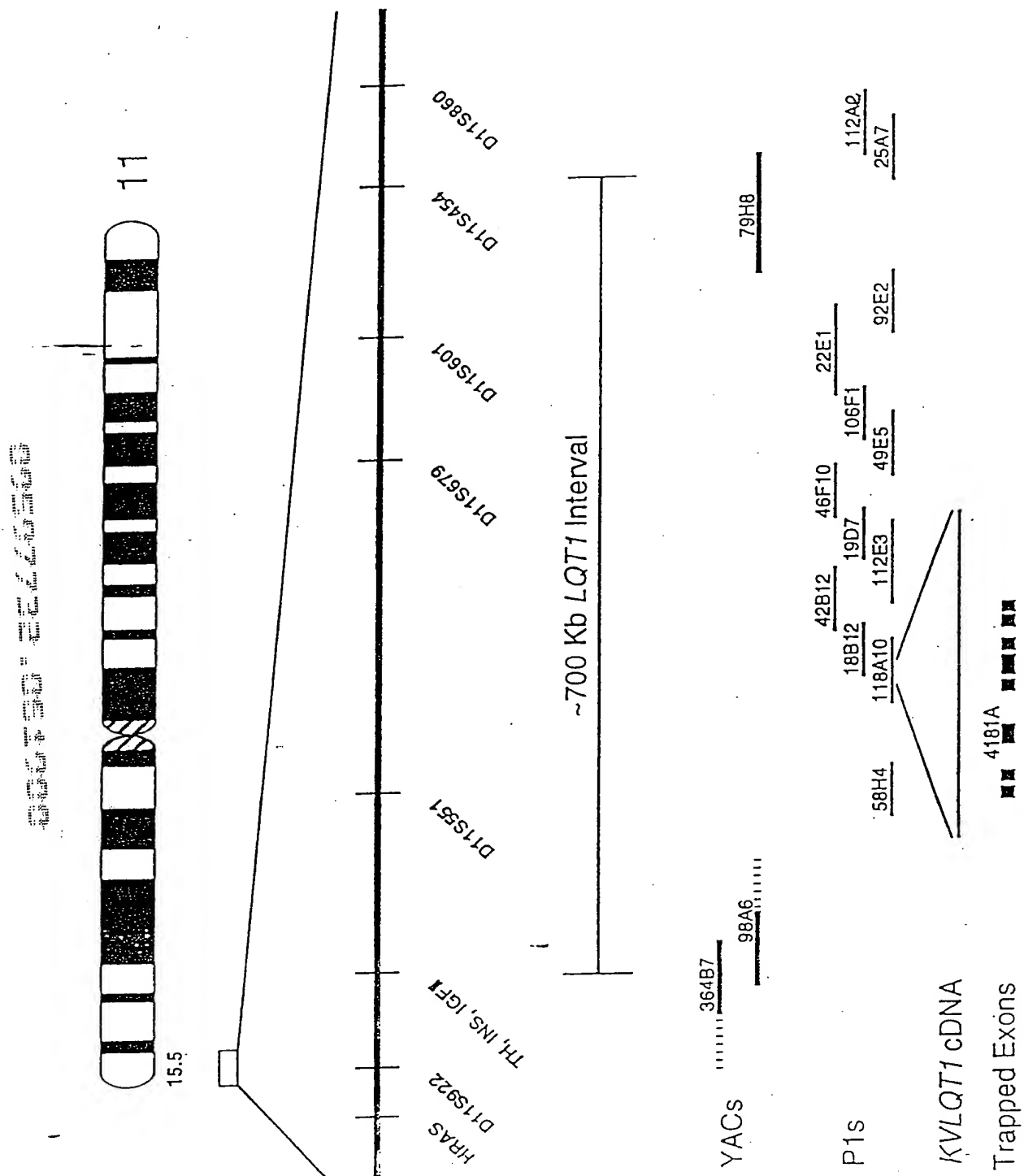


Figure 2

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

EVLOT1 1 FLIVLCLIFSVLSTIEQYAAATGT.....LPMHEIVLVVFFGTEVVRWLSACRSKYVGLWGBLRFARPIISIDLIWVASHWVLCVG.....SKQVFAI-95
ONSUAXEI 237 HLLSVLELETLPEFNKYRVFTTTGTGKIEEDEVPDITDPELLETLCLITTELETVRELACF.....HKLNFCRDVRNVIDIALIPEYETJLATWAEEDTLMLPKAPVSPQDKSSHQNSL-358
81 82 83
SAIRGIRFLQILRLHIVDROGCTWRLLGSVFTIRQELITTLTYIGFLGLIFSSYFVYLAEKDANVESGRVEFGSYADALHMGWVTTTIGYGDKVPQTVWVKTIASCFSVFAISFFALPAGILGSGFAL-224
84 85 86
AHLRVHVAZVPELKLSEHSKGIQLGRTLXASHRELGLLIEELEIGVGLLESSAVYPAEAGSENSF....FKSIPDAENMAVTHTVGYGHTFVGMCKINGSLCWAGVLTIALPUPVIVSNFY-483
84 85 86
Pore

Figure 3

3.2 kb →

Heart
Brain
Placenta
Lung
Liver
Skeletal muscle
Kidney
Pancreas

Figure 4

CTGCCCCCTCCGGCCCCGCCCCGAGCGCCCGGGCTGGGCCGGCAGCGCCCCCGCGGGGGCTGGCAGCAGTGGCTGCC-81
 CGCACTGCGCCCCGGGCGCTCGCCTTCGCTGCAGCTCCCGTGCCGCGCGTTCGGGCGGGCCCCCGGCAGGCCCTCCTCGTT-162
 ATGGCCGCGGCTCCTCCCCGCCCAGGGCCGAGAGGAAGCGCTGGGGTTGGGGCGCGCTGCCAGGCGCCGGCGGGGAGC-243
 M A A A S S P P R A E R K R W G W G R L P G A R R G S -27
 GCGGGCTGGCCAAGAAGTGGCCCTTCTCGCTGGAGCTGGCGGAGGGCGGCCCGGGCGGGCGCGCTCTACGCGCCCATC-324
 A G L A K K C P F S L E L A E G G P A G G A L Y A P I -54
 GCGCCCGGCGCCCCAGGTCCCCGCGCCCCCTGCGTCCCCGCGCGCGCCCCCGCGCCCCCAGTTGCCCTCCGACCTTGGCCCG-405
 A P G A P G P A P P A S P A A P A A P P V A S D L G P -81
 CGGCCGCGGTGAGCCTAGACCCGCGCGTCTCCATCTACAGCACGCGCCGCGCGGTGTGGCGCGCACCCACGTCCAGGGC-486
 R P P V S L D P R V S I Y S T R R P V L A R T H V Q G -108
 CGCGTCTACAACCTCCTCGAGCGTCCCACCGGTGGAAATGCTTCGTTTACCACTTCGCCGTCTCCTCATCGTCTGGTC-567
 R V Y N F L E R P T G W K C F V Y H F A V F L I V L V -135
 TGCCTCATCTTCAGCGTGTGTCCACCATCGAGCAGTATGCCGCCCTGGCCACGGGACTCTCTTCTGGATGGAGATCGTG-648
 C L I F S V L S T I E Q Y A A L A T G T L F W M E I V -162
 CTGGTGGTGTCTTCTCGGGACGGAGTACGTGGTCCGCCTCTGGTCCGCGCGGTGCCGCGAGCAAGTACGTGGGCCTCTGGGG-729
 L V V F E G T E Y V V R L W S A G C R S K Y V G L W G -189
 CGGCTGCGCTTTGCCCCGAAGCCCATTTCCATCATCGACCTCATCGTGGTGTGGCTCCATGGTGGTCTCTGCGTGGGC-810
 R L R F A R K P I S I I D L I V V V A S M V V L C V G -216
 TCCAAGGGGCGAGTGTTCGCCACGTCCGCCATCAGGGGCATCCGCTTCCTGCAGATCCTGAGGATGCTACACGTGACCGC-891
 S K G Q V F A T S A I R G I R F L Q I L R M L H V D R -243
 CAGGGAGGCACCTGGAGGCTCCTGGGCTCCGTGGTCTTCATCCACCGCCAGGAGCTGATAACCACCCTGTACATCGCTTC-972
 Q G G T W R L L G S V V F I H R Q E L I T T L Y I G F -270
 CTGGGCTCATCTTCTCCTCGTACTTTGTGTACCTGGCTGAGAAGGACGCGGTGAACGAGTCAGGCCGCGTGGAGTTCCGGC-1053
 L I G L I F S S Y F V Y L A E K D A V N E S G R V E F G -297
 AGGTACGCAGATGCGCTGTGGTGGGGGGTGGTCACAGTCACCACCATCGGCTATGGGGACAAGGTGCCCCAGACGTGGGTC-1134
 S Y A D A L W W G V V T V T T I G Y G D K V P Q T W V -324
 GGAAGACCATCGCCTCCTGCTTCTGTCTTTGCCATCTCCTTCTTTGCGCTCCCAGCGGGATTCTTGGCTCGGGGTTT-1215
 G K T I A S C F S V F A I S F F A L P A G I L G S G F -351
 GCCCTGAAGGTGCAGCAGAAGCAGAGGCAGAAGCACTTCAACCGGCAGATCCCGGCGGCAGCCTCACTCATTACAGACCGCA-1296
 A L K V Q Q K Q R Q K H F N R Q I P A A A S L I Q T A -378
 TGCAGGTGCTATGCTGCCGAGAACCCCGACTCCTCCACCTGGAAGATCTACATCCGGAAGGCCCCCGAGCCACACTCTG-1377
 W R C Y A A E N P D S S T W K I Y I R K A P R S H T L -405
 CTGTACCCAGCCCCAAACCCAAGAAGTCTGTGGTGGTAAAGAAAAAAGTTCAAGCTGGACAAAGACAATGGGGTGA-1458
 L S P S P K P K K S V V V K K K K F K L D K D N G V T -432
 CCTGGAGAGAAGATGCTCACAGTCCCCCATATCACGTGCGACCCCCCAGAAGAGCGGCGGTGGACCACTTCTCTGTGCGAC-1539
 P G E K M L T V P H I T C D P P E E R R L D H F S V D -459
 GGCTATGACAGTTCTGTAAGGAAGAGCCCAACACTGCTGGAAGTGAGCATGCCCATTTTCATGAGAACCAACAGCTTCGCC-1620
 G Y D S S V R K S P T L L E V S M P H F M R T N S F A -486
 GAGGACCTGGACCTGGAAGGGGAGACTCTGCTGACACCCATCACCCACATCTCACAGCTGCGGGAACACCATCGGGCCACC-1701
 E D L D L E G E T L L T P I T H I S Q L R E H H R A T -513
 ATTAAGGTCATTGACGCATGCACTACTTTGTGGCCAAGAAGAAATTCAGCAAGCGCGGAAGCCTTACGATGTGCGGGAC-1782
 I K V I R R M Q Y F V A K K K F Q Q A R K P Y D V R D -540
 GTCATTGAGCAGTACTCGCAGGGCCACCTCAACCTCATGGTGGCATCAAGGAGCTGCAGAGGAGCTGGACCACTGTCATT-1863
 V I E Q Y S Q G H L N L M V R I K E L Q R R L D Q S I -567

Figure 5A

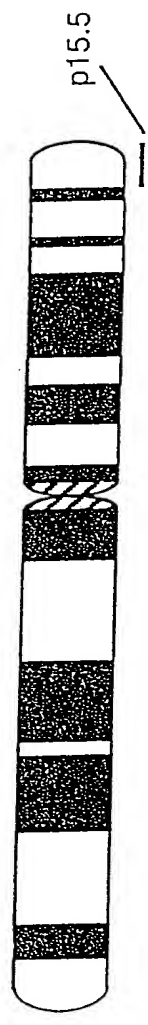
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G K P S L F I S V S E K S N D R G S N T I G A R L N R -594

GTAGAAGACAAGGTGACGCAGCTGGACCAGAGGCTGGCACTCATCACCGACATGCTTACCAGCTGCTCTCCTTGACCGGT-2025
V E D K V T Q L D Q R L A L I T D M L H Q L L S L H G -621
GGCAGCACCCCCGGCAGCGCGGCCCCCCCCAGAGAGGGCGGGGCCACATCACCCAGCCCTGCGGCAGTGGCGGCTCCGTC-2106
G S T P G S G G P P R E G G A H I T Q P C G S G G S V -648
GACCTGAGCTCTTCTGCCCAGCAACACCCTGCCCACCTACGAGCAGCTGACCGTGCCAGGAGGGGGCCCGATGAGGGG-2187
D P E L F L P S N T L P T Y E Q L T V P R R G P D E G -675
TCCTGAGGAGGGGATGGGGCTGGGGGATGGGCCTGAGTGAGAGGGGAGGCCAAGAGTGGCCCCACCTGGCCCTCTCTGAAG-2268
S * -676
GAGGCCACCTCCTAAAAGGCCAGAGAGAAGAGCCCCACTCTCAGAGGCCCAATACCCCATGGACCATGCTGTCTGGCAC-2349
AGCCTGCACTTGGGGGCTCAGCAAGGCCACCTCTTCTGCGCGGTGTGGGGGCCCCGTCTCAGGTCTGAGTTGTTACCCCA-2430
AGCGCCCTGGCCCCACATGGTGATGTTGACATCACTGGCATGGTGGTTGGGACCCAGTGGCAGGGCACAGGGCCTGGCCC-2511
ATGTATGGCCAGGAAGTAGCACAGGCTGAGTGCAGGCCCCACCTGCTTGGCCCAGGGGGCTTCTGAGGGGAGACAGAGCA-2592
ACCCCTGGACCCACGCTCAAATCCAGGACCCTGCCAGGCACAGGCAGGGCAGGACCAGCCCACGCTGACTACAGGGCCAC-2673
CGGCAATAAAAGCCCAGGAGCCCATTTGGAGGGCCTGGGCCTGGCTCCCTCACTCTCAGGAAATGCTGACCCATGGGCAGG-2754
AGACTGTGGAGACTGCTCCTGAGCCCCCAGCTTCCAGCAGGAGGGACAGTCTCACCATTTCGCCAGGGCACGTGGTTGAGT-2835
GGGGGGAACGCCCACCTTCCCTGGGTAGACTGCCAGCTCTTCTAGCTGGAGAGGAGCCCTGCCTCTCCGCCCTGAGCCC-2916
ACTGTGCGTGGGGCTCCCGCCTCCAACCCCTCGCCCAGTCCCAGCAGCCAGCCAAACACACAGAAGGGGACTGCCACCTCC-2997
CCTTGCCAGCTGCTGAGCCGAGAGAAGTGACGGTTCTTACACAGGACAGGGGTTCTTCTGGGCATTACATCGCATAGAA-3078
ATCAATAATTTGTGGTGATTGATCTGTGTTTTAATGAGTTTCACAGTGTGATTTGATTATTAATGTGCAAGCTTTTC-3159
CTAATAAACGTGGAGAATCAC (A)n -3180

Figure 5B

118A10 42B12 19D7 46F10 49E5

chromosome 11



118A10

42B12

19D7

49E5

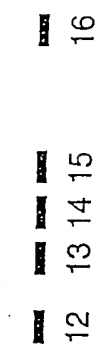
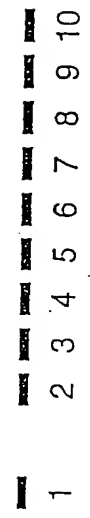
cos1

18B12

112E3

46F10

genomic clones



KVLQ1 exons

Figure 6

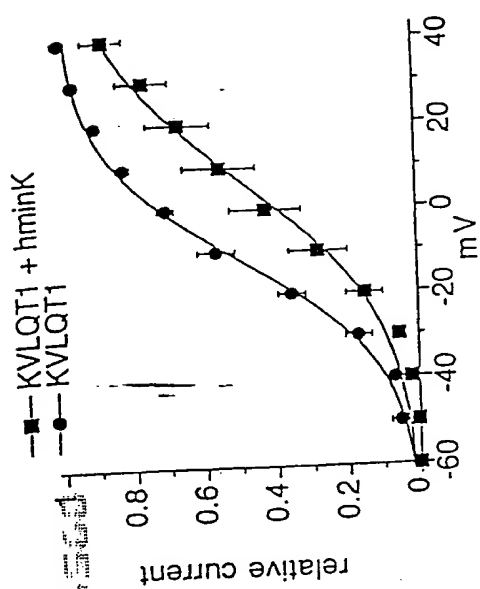


Figure 7A

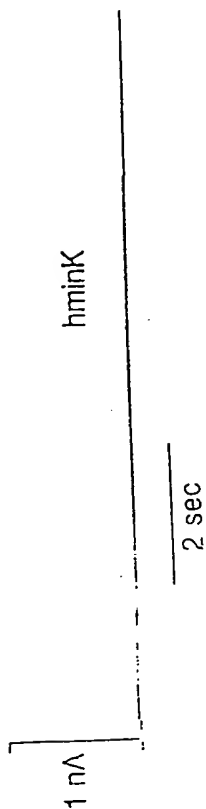


Figure 7B

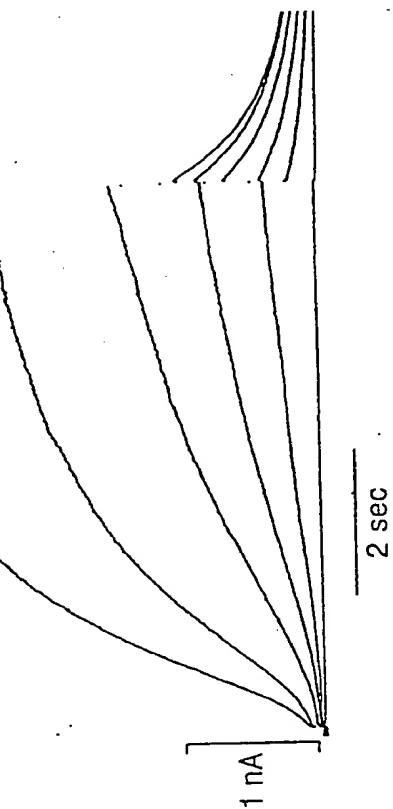


Figure 7C

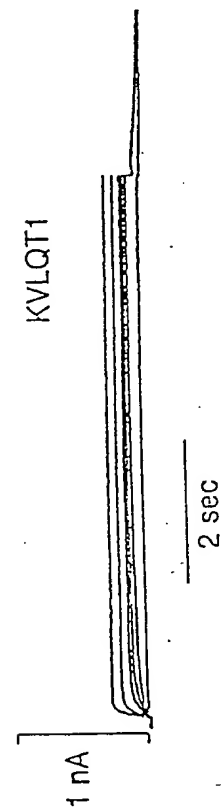


Figure 7D

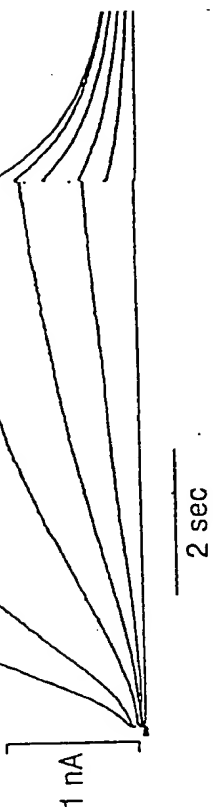


Figure 7E

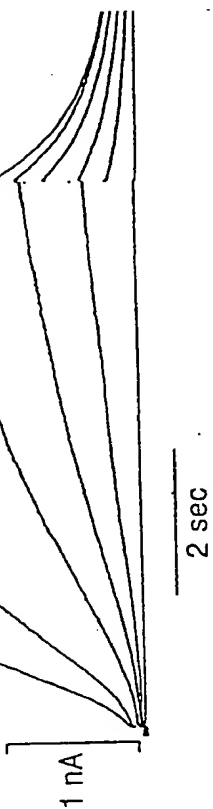


Figure 7F

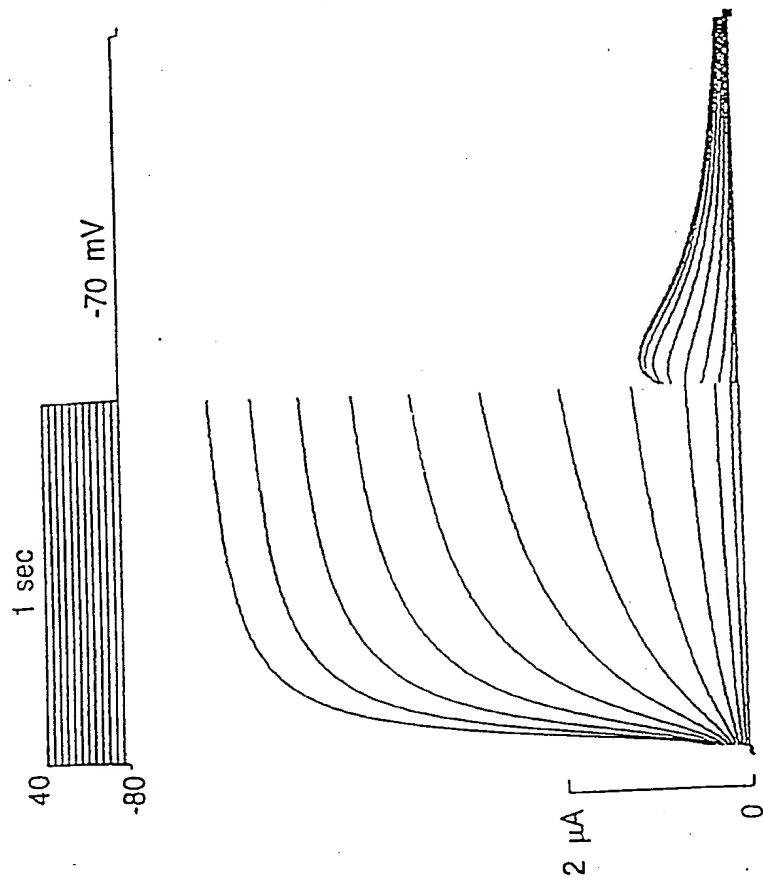


Figure 8A

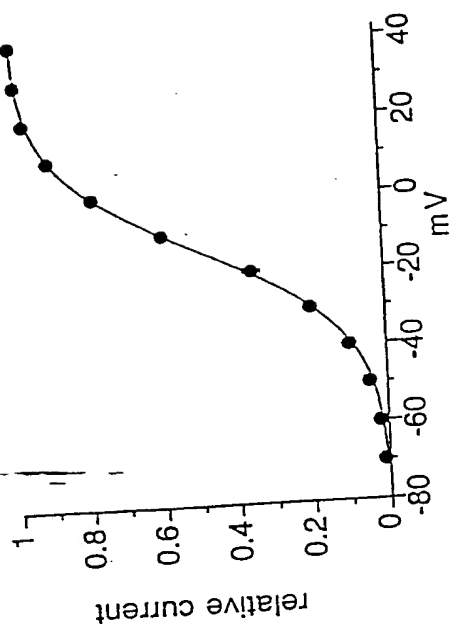


Figure 8B

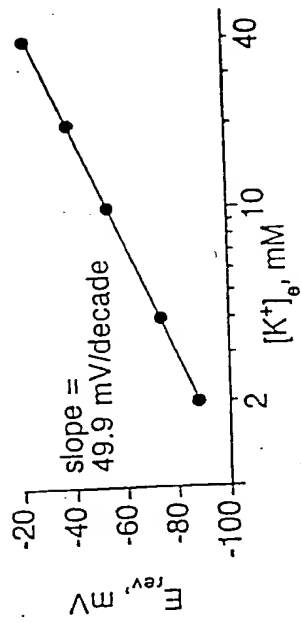


Figure 8C

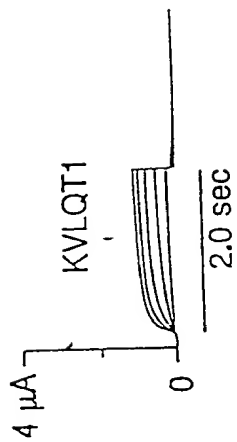


Figure 9A

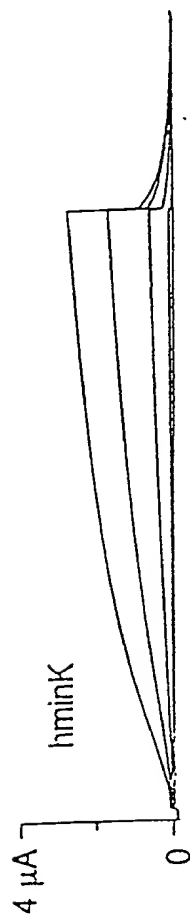


Figure 9B

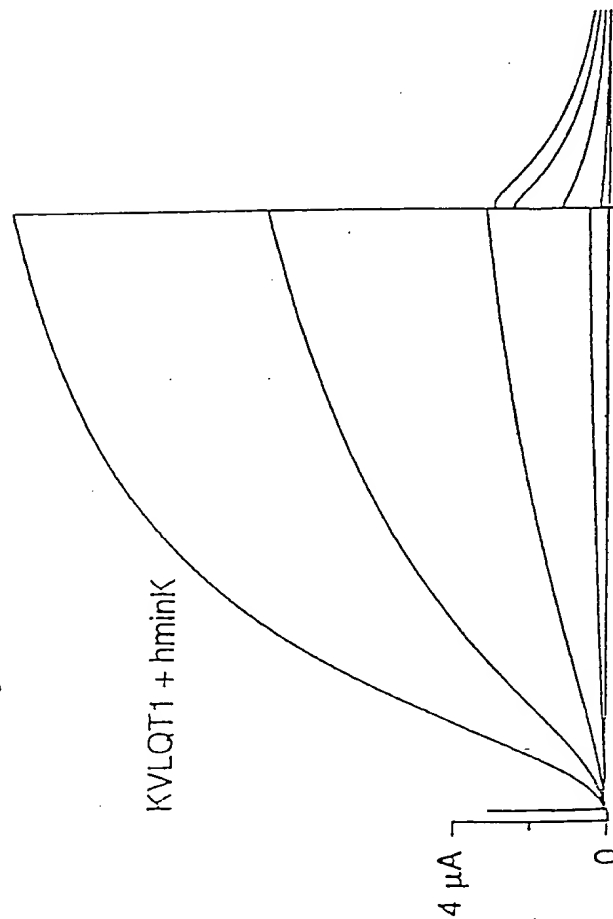


Figure 9C

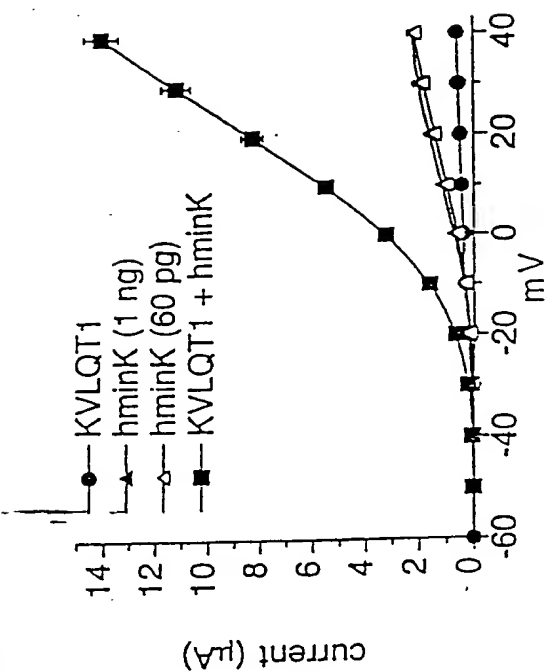


Figure 9D

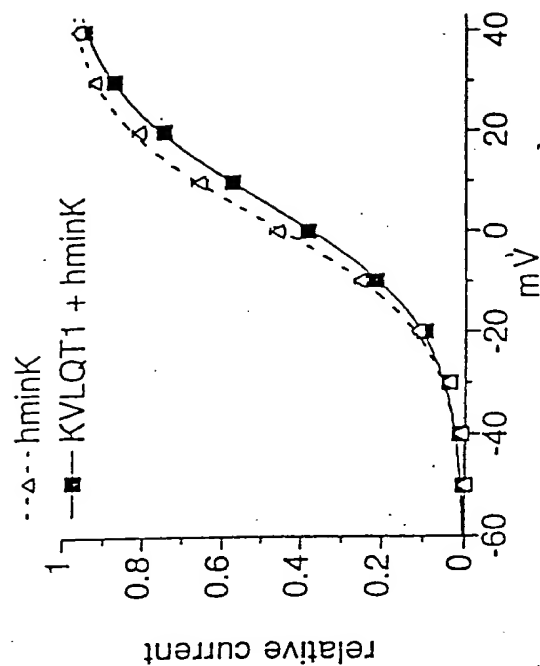
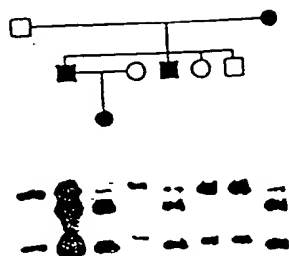


Figure 9E

Xenopus	MNENAINSLYEAIPLPDGSSNGQRQEDRQANSFELKRETLVATDPPRPT
Human	QGRVYNFLERPTGWKCFVYHFAVFLIVL
Xenopus	INLDP RVSIYSGRRPLFSRTNIQGRVYNFLERPTGWKCFVYHFTVFLIVL
Human	S1 _____ S2 _____ VCLIFSVLSTIEQYAALATGTLFWMEIVLVVFFGTEYVVRLWSAGCRSKY
Xenopus	ICLIFSVLSTIQYNNLATETLEFWMEIVLVVFFGAEYVVRLWSAGCRSKY
Human	_____ S3 _____ S4 _____ VGLWGRLRFARKPISIDLVVVASMVVLCVSGKGQVFATSAIRGIRFLQ
Xenopus	VGWVGRLRFARKPISVIDLVVVASVIVLCVGSNGQVFATSAIRGIRFLQ
Human	_____ S5 _____ ILRMLHVDROGGTWRLGSSVFIHRQELITTLYIGFLGLIFSSYFVYLAE
Xenopus	ILRMLHVDROGGTWRLGSSVFIHRQELITTLYIGFLGLIFSSYFVYLAE
Human	_____ Pore _____ KDAVNESGRVEFGSYADALWVGVTVTITIGYGDKVPQTWVGKTIASCFSV
Xenopus	KDAIDSSGEYQFGSYADALWVGVTVTITIGYGDKVPQTWVGKTIASCFSV
Human	_____ S6 _____ FAISFFALPAGILGSGFALKVQKQKQKHFNRIQIPAAASLIQTAWRCYAA
Xenopus	FAISFFALPAGILGSGFALKVQKQKQKHFNRIQIPAAASLIQTAWRCYAA
Human	ENPDSSTWKIYIRKAPRSHTLLSPSPKPKSVVVKKKFKLDKONGVTPG
Xenopus	ENPD SATWKIYIRKQSRNHIMSPSP
Human	EKMLTVPHITCDPPEERRLDHFSVDGYDSSVRKSPITLLEVSMPHFMRNS
Human	FAEDLDLEGETLLTPITHISQLREHHRATIKVIRRMQYFVAKKKFQQARK
Human	PYDVRDVIEQYSQGHNLNMRVIKELQRRLDQSIGKPSLFI SVSEKSKDRG
Human	SNTIGARLNRVEDKVTQLDQRLALITDMLHQLLSLHGGSTPGSGGPPREG
Human	GAHITQPCGSGGSVDPELFLPSNTLPTYEQLTVPRRGFDEGS

Figure 10

K1532



K2605

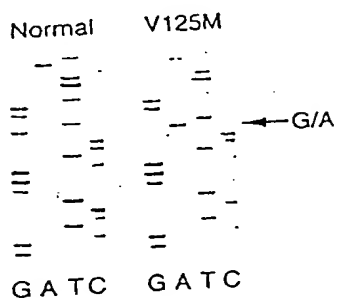
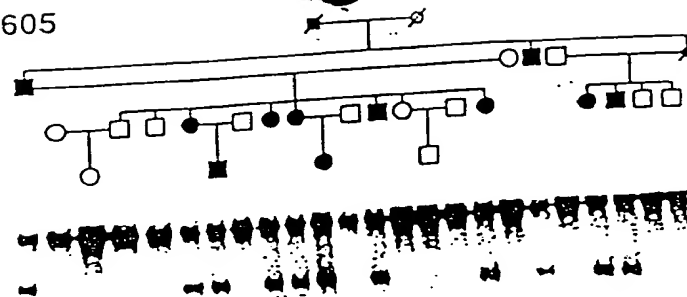


Figure 11A

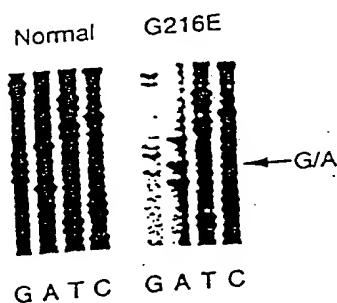
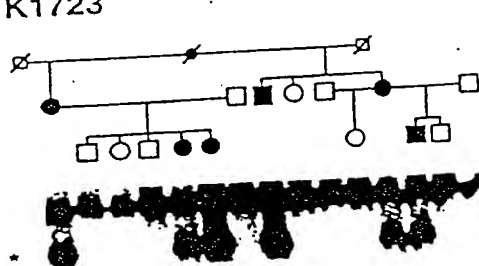


Figure 11B

K1723



K1807

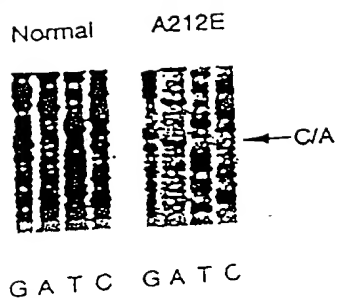
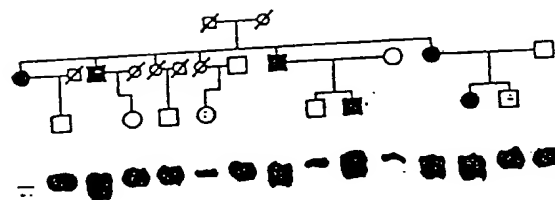


Figure 11C

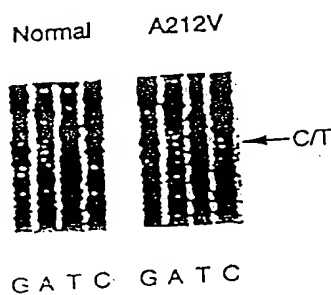


Figure 11D

K13216

K1777

K20925

K2557

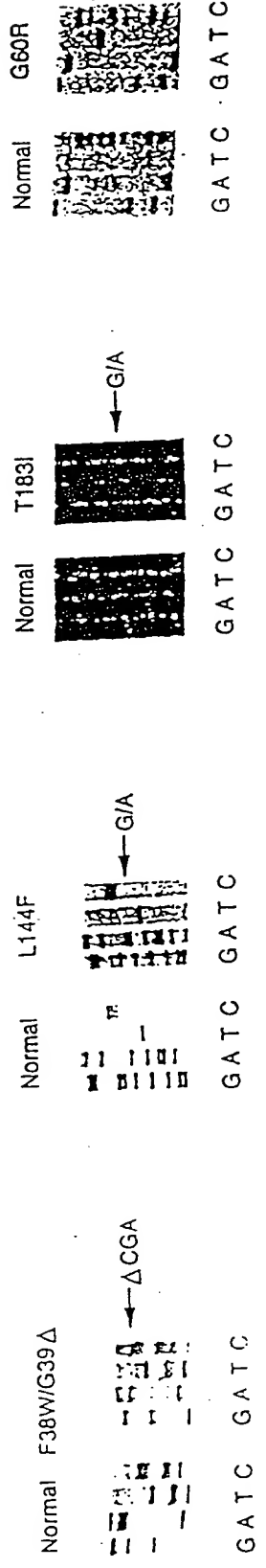


Figure 12A

K13119

K20926

K15019

Figure 12D

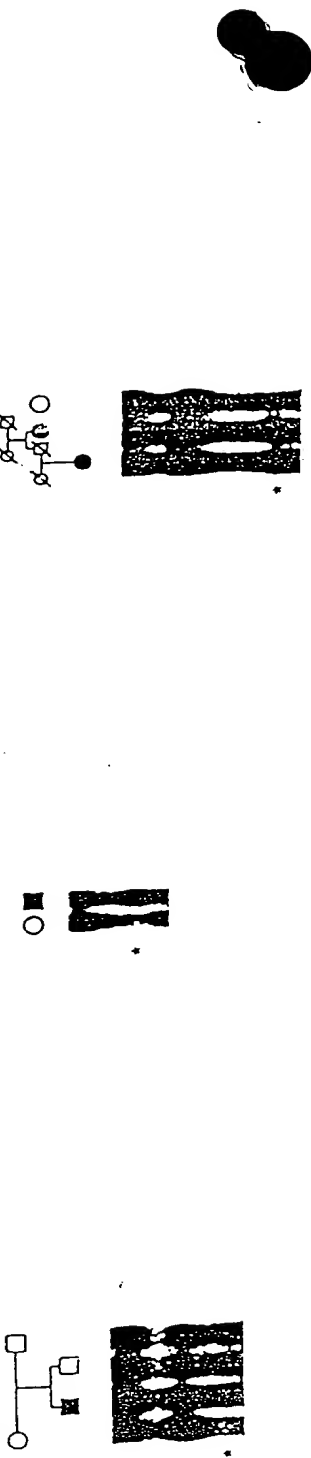


Figure 12C

Figure 12B

Normal

Normal

Normal

Normal

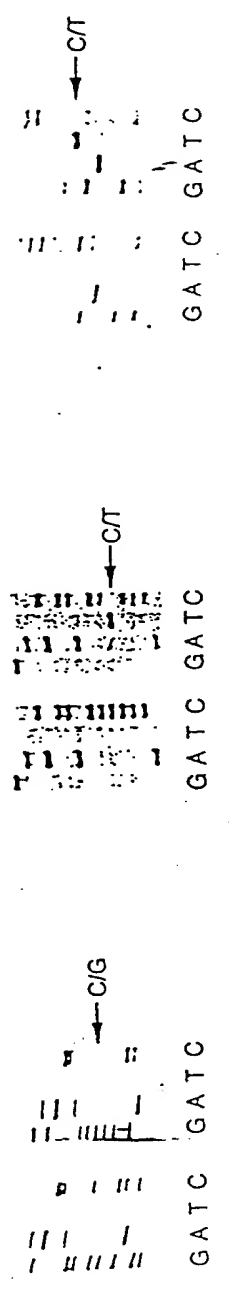
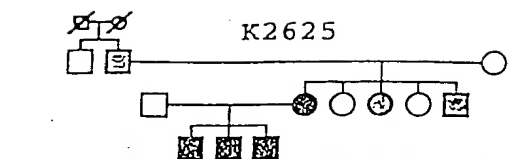


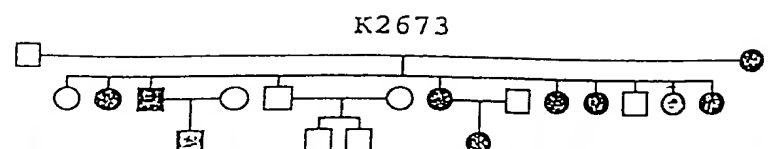
Figure 12E

Figure 12F

Figure 12G



K2625



K2673



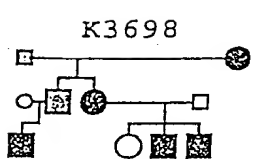
Gly168Arg

Figure 12H



Gly168Arg

Figure 12I



K3698



Gly168Arg

Figure 12J

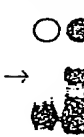
K19187



Gly314Ser

Figure 12K

K22709



Tyr315Cys

Figure 12L

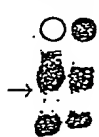
K2762



Lys318Asn

Figure 12M

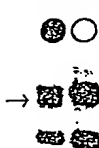
K3401



Leu353Pro

Figure 12N

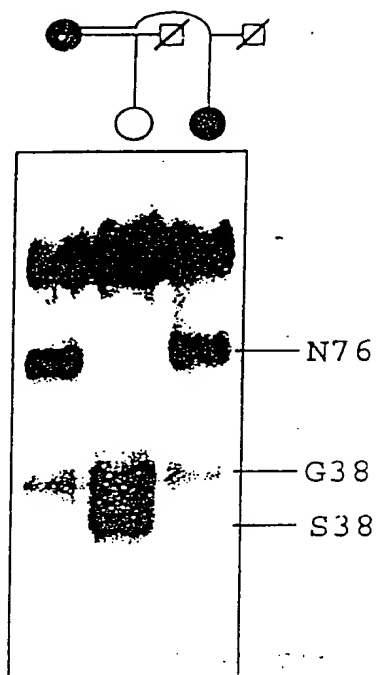
K2824



Arg366Trp

Figure 12O

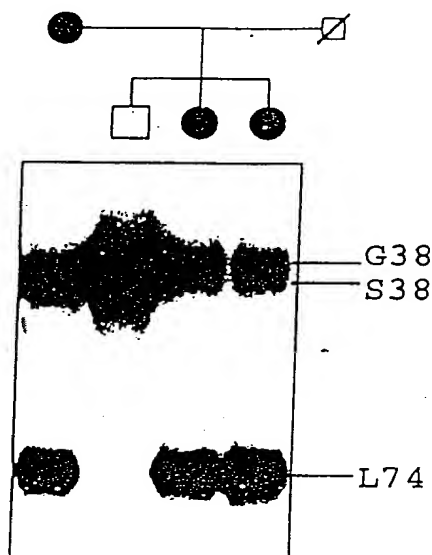
K1789



Normal	CAC	TCG	AAC	GAC	CCA	TTC	AAC
	H	S	N	D	P	F	N
				↓			
Mutant	CAC	TCG	AAC	AAC	CCA	TTC	AAC
	H	S	N	N	P	F	N

Figure 13A

K1754



Normal	CTG	GAG	CAC	TCG	AAC	GAC	CCA
	L	E	H	S	N	D	P
				↓			
Mutant	CTG	GAG	CAC	TTG	AAC	GAC	CCA
	L	E	H	L	N	D	P

Figure 13B

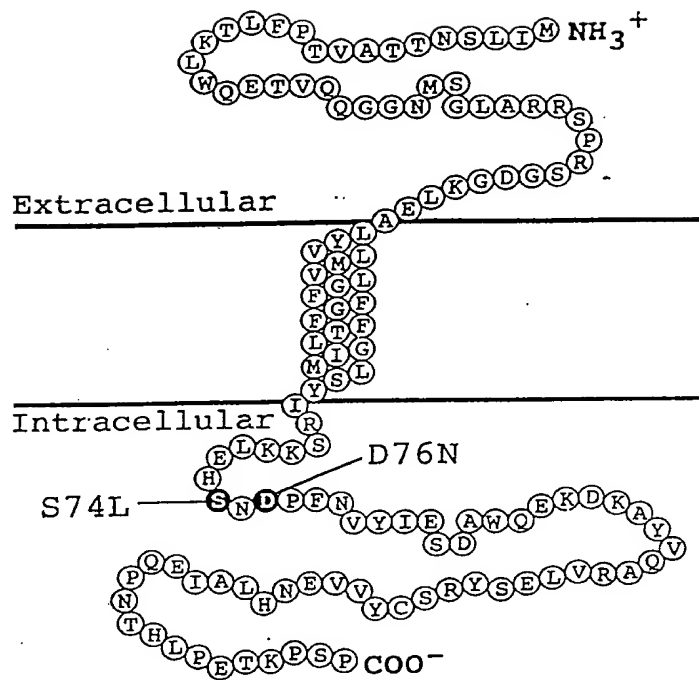


Figure 13C

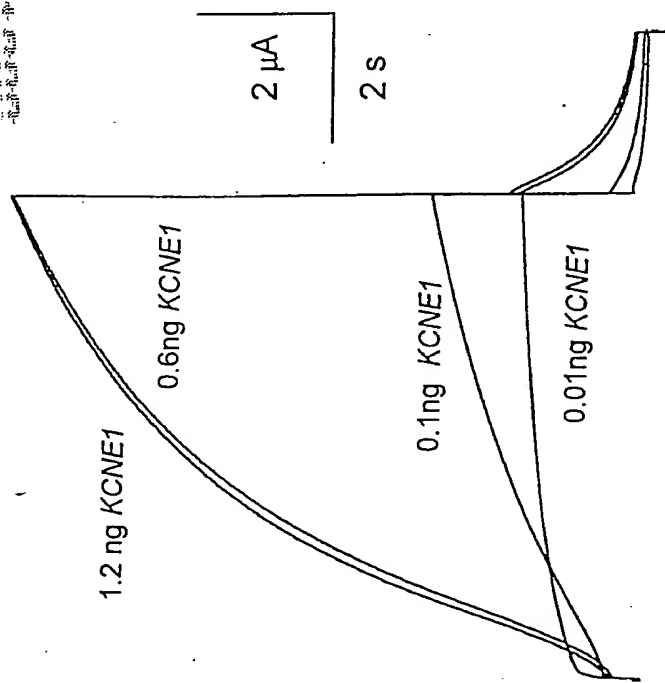


Figure 14A

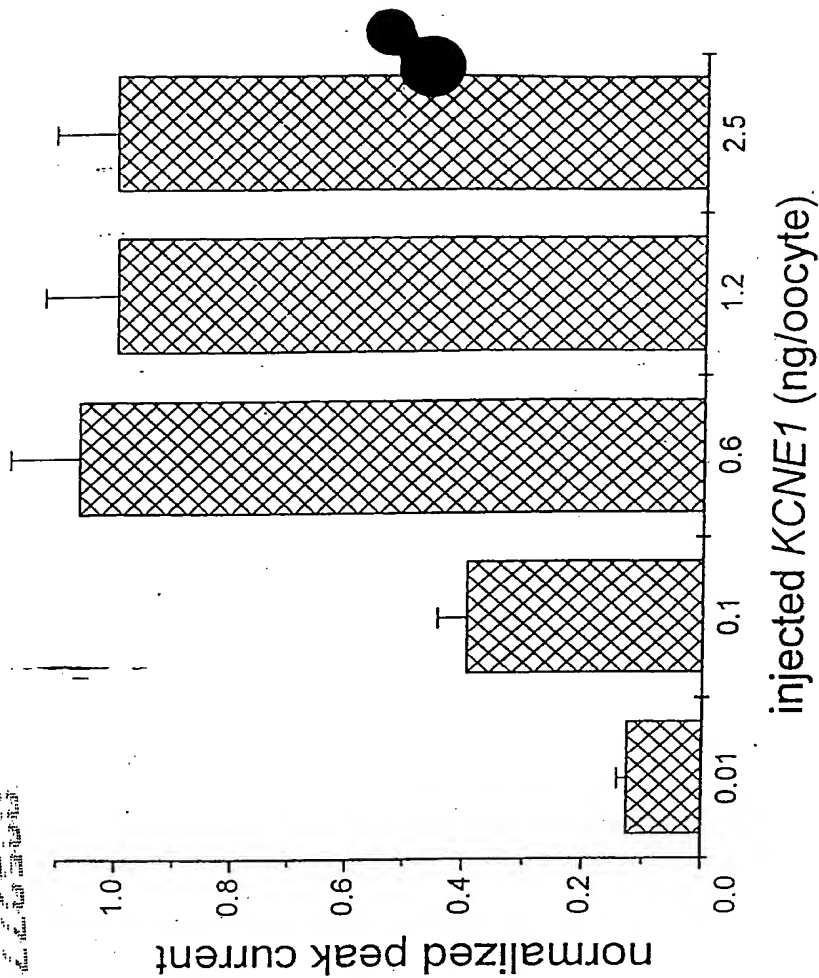


Figure 14B

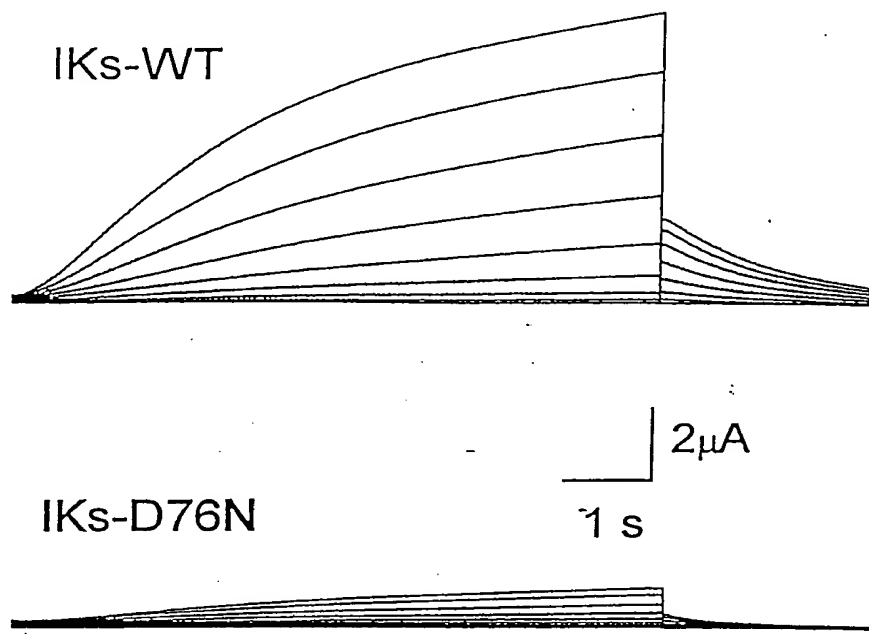


Figure 15A

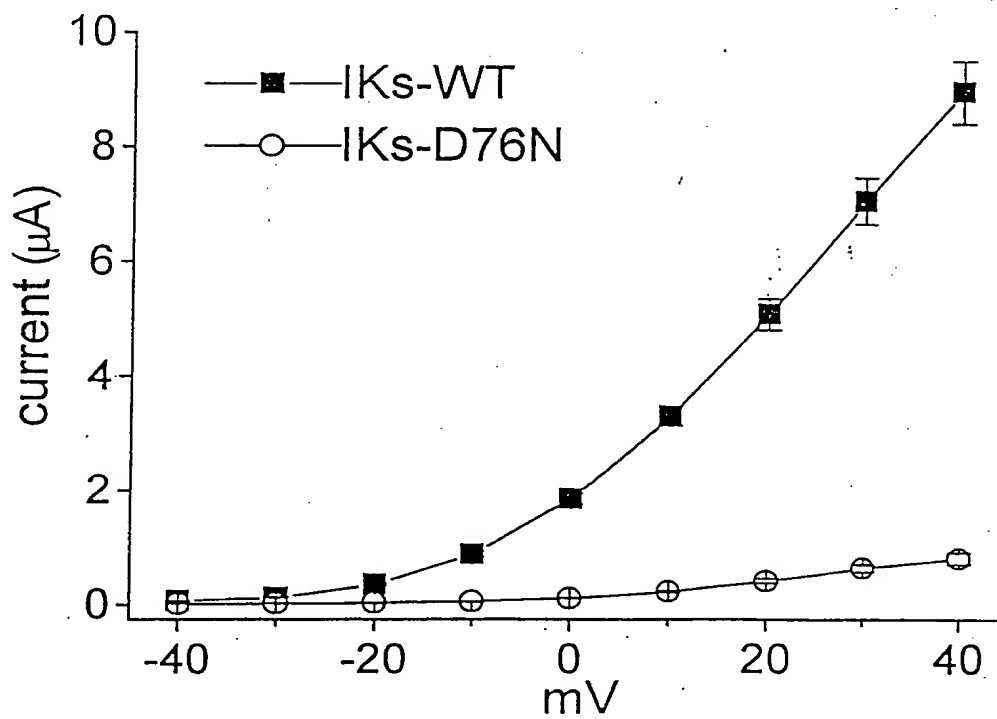


Figure 15B

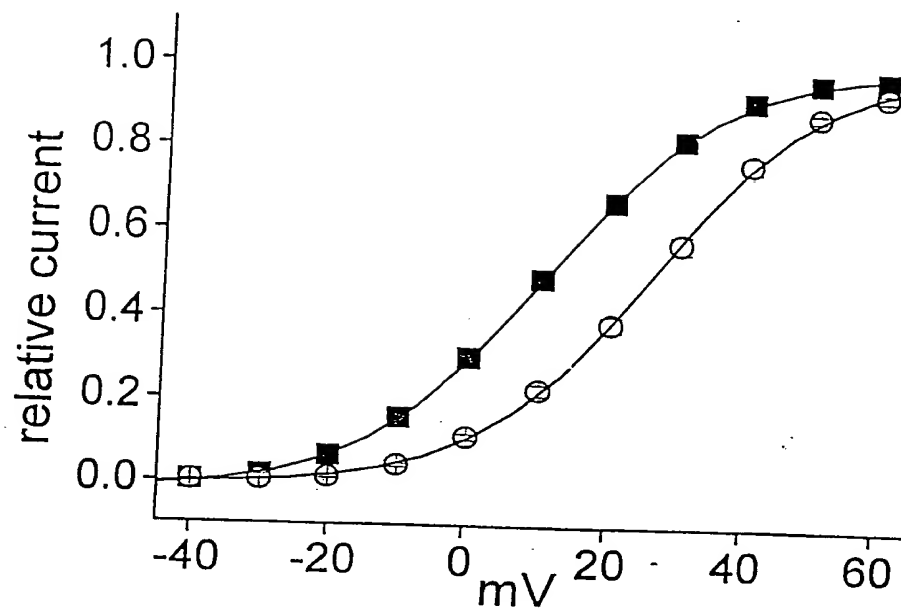


Figure 15C

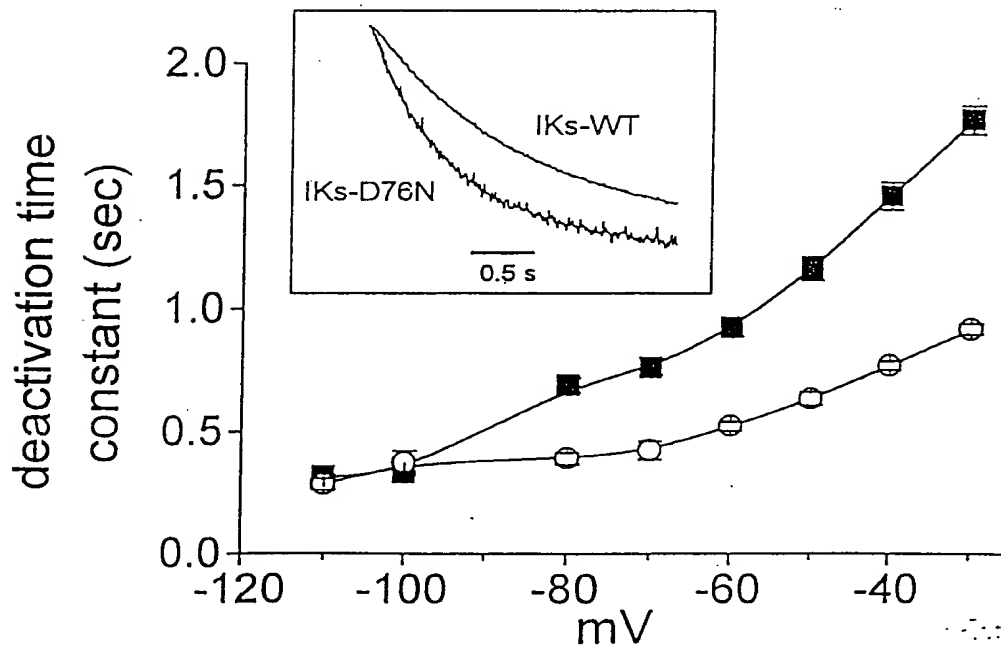


Figure 15D

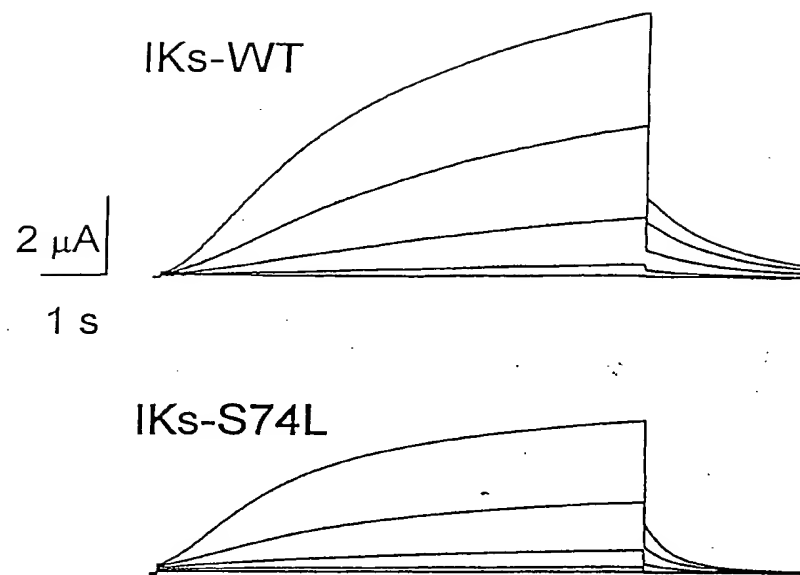


Figure 16A

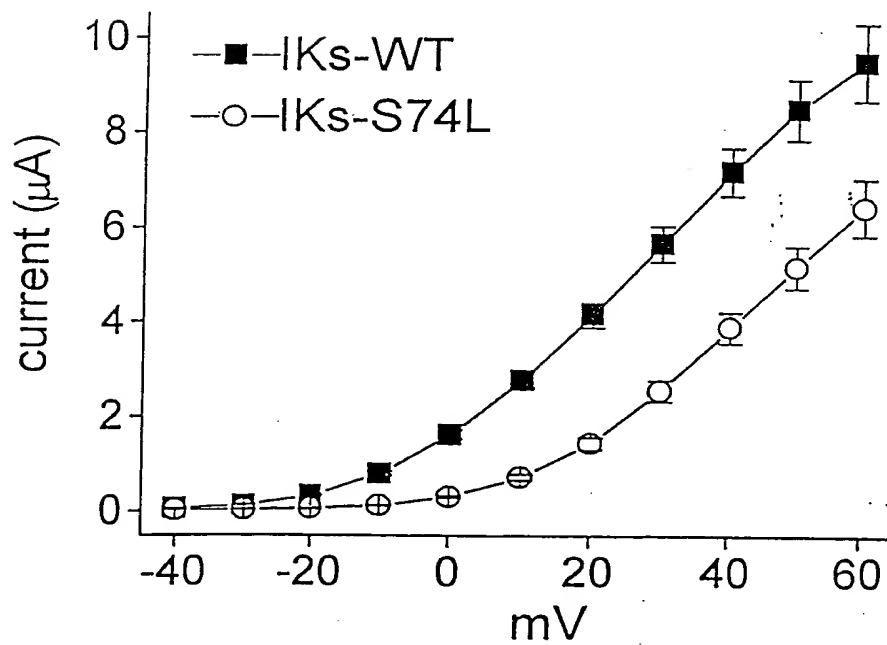


Figure 16B

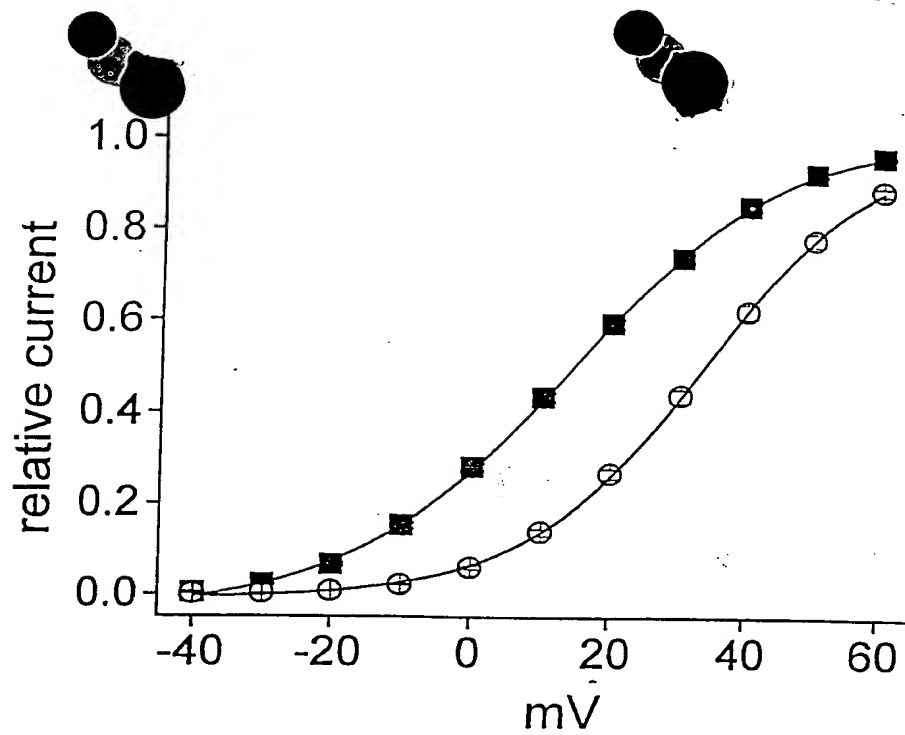


Figure 16C

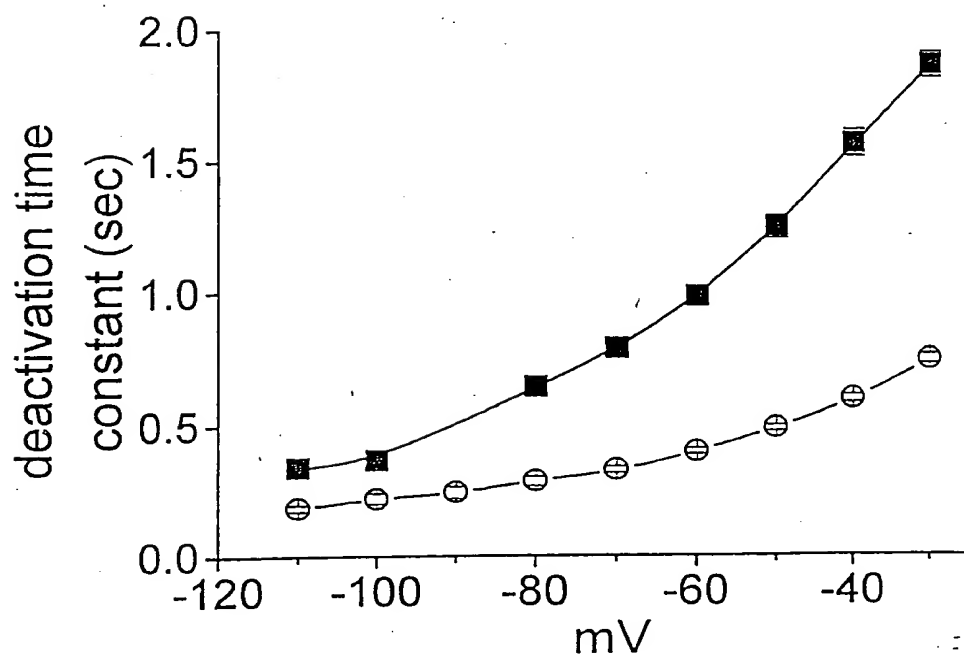


Figure 16D

q22.1-q22.2

chromosome 21



~60 kb

cos2

cos1

genomic clones

KCNE1 exons

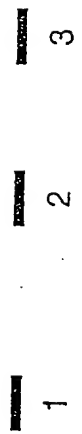


Figure 17

ACACCCGGCTCTCTCGGCATCTCAGACCCGGGAAAAATCCTCTGCTTTCTCTGGCCAGTTTCACACAATCATCAGGTGAG-81
 CCCGAGGATCCATTGGAGGAAGGCATTATCTGTATCCAGAGGAAATAGCCAAGGATATTTCAGAGGTGTGCCTGGGAAGTTTG-162
 AGCTGCAGCAGTGGAACCTTAATGCCCAGGATGATCTGTCTAACACCACAGCGGTGACGCCCTTTCTGACCAAGCTGTGG-243
 M I L S N T T A V T P F L T K L W -17
 CAGGAGACAGTTCAGCAGGGTGGCAACATGTCGGGCTGGCCCGCAGGTCCCCCGCAGCGGTGACGGCAAGCTGGAGGCC-324
 Q E T V Q Q G G N M S G L A R R S P R S G D G K L E A -44
 CTCTACGTCTCATGGTACTGGGATTCTTCGGCTTCTTCACCCTGGGCATCATGCTGAGCTACATCCGCTCCAAGAAGCTG-405
 L Y V L M V L G F F G F F T L G I M L S Y I R S K K L -71
 GAGCACTCGAACGACCCATTCAACGTCTACATCGAGTCCGATGCCCTGGCAAGAGAAGGACAAGGCCCTATGTCCAGGCCCGG-486
 E H S N D P F N V Y I E S D A W Q E K D K A Y V Q A R -98
 GTCCTGGAGAGCTACAGGTGCTGCTATGTCGTTGAAAACCATCTGGCCATAGAACAACCCAACACACACCTTCTGAGACG-567
 V L E S Y R S C Y V V E N H L A I E Q P N T H L P E T -125
 AAGCCTTCCCCATGAACCCCACTGGCTAAACTGGACACCTCCTGCTGGNNNNNAGATTTTCTAATCACATTCCTCTCA-648
 K P S P *
 TACTCTTTATGTGATGGATACCACTGGATTTCTTTTTGGCTGTTGTAANGGTGAGGGGTGGATTAATGACACTGTTTCA-729
 CTGTTTCTCTAAATCACGTTCTTTTGTGATAGACTGTCAGTGGTTCCCCCATATCTGTCCCTGCCCTTGCTAAATTTAGCA-810
 GAATCCCTGAGGACATGGCCTCTGAGAATAGCAGCTGCATTTCACACTCCCTTGACGCTAGCAAGGTTGTGTGACTAAG-891
 CCTGGCCAGTAGGCATGGAAGTGAAGACTGTAATGTCCAAGTAATCCTTGGAAAGAAAAGAACGTGCCCTTAACCTA-972
 TGTCTGCTTCCAGTGGCTGGATGTGGAGGAGGTGGAGACAGTATGAGACTGGGAAAGTTGCGGGCACTCAAAGAGCC-1053
 ACACACATCTGGGCTGGGCGACGTGGATCCTCCTTACCACCCACCAGGCCAGATTTACAGGAGAGAGAAATCCACTCCAC-1134
 TCTTCTTAAGCCACTGTTATTCTGATCTCTGTTAAGGTGCGAGAATCAATGCCCTTACTGATACACCTACCTTATAGGAC-1215
 TGAACCTAAAGGCATGACATTTCCATACTTGTGCACAGCACACACTGATTCTGCCCTTGTCACTTCTGTGCTCACTCTTGT-1296
 GGCTCTATCCTCCTCCTGCCCTTCCGCCTTCCACTCCTCCCTTGCACCCATCCTGCACACATCTCCCTGAAAACACACAGG-1377
 CACATACACTCATATACATAGACACACATACACCTCAATCTAGAAAGAACTTGCTTTGTACAGGGCTGAGATGGAGGAG-1458
 AAAAAAATGCCCCCTTCAAGATGCATACCAAGGGGAAGGTGCTCGGTCACTGTGGGAGCAGGGAAGGTGCCCCCACTCCC-1539
 CGAGAGCCAGGGGAAGGAGTGGCTCTGGGCAGAGAGGGACACATAGCACTGGGGTGGCAGGTCTTTTGAGGTGATGGGCC-1620
 GGTTTTGTGAGATGAATTGTATCCCCCAAAAGACAGGTACCTTCAATGTGACCTAATTGGGAAATAGAGTCTTTGCAGAT-1701
 G(A)n -1702

Figure 18